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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,253	01/26/2005	Samuel Weiss	16601-021US1	8661

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EXAMINER	
QIAN, CELINE X	
ART UNIT	PAPER NUMBER
1636	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,253	WEISS, SAMUEL	
	Examiner	Art Unit	
	CELINE X. QIAN	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 6-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 6-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 January 2005* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 6-9 are pending in the application.

Response to Amendment

The amendment filed on 3/21/07 has been entered.

The finality of the office action mailed on 10/15/07 has been withdrawn in view of the new ground of rejection discussed below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing oligodendrocytes from mammalian multipotent neural stem cells comprising: providing a cell culture of multipotent neural stem cells with an effective amount of granulocyte-macrophage colony stimulating factor under the conditions that result in production of oligodendrocytes from the multipotent neural stem cells, does not reasonably provide enablement for a method of producing oligodendrocytes from mammalian multipotent neural stem cells by contacting a cell culture of multipotent stem cells obtained from neural tissue with other factors such as IL-3 or IL-5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement

and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

The nature of the invention

The claims are drawn to a method of producing oligodendrocytes from mammalian multipotent neural stem cells by contacting a cell culture of multipotent neural stem cells obtained from neural tissue with an effective amount of at least one oligodendrocyte promoting factor, wherein said factor is selected from the group consisting of GM-CSF, IL-3 and IL-5.

The breadth of the scope and the teaching from the instant specification

The claimed breadth encompasses inducing the differentiation of multipotent neural stem cells by one or more of the factor of GM-CSF, IL-3 and IL-5. However, the instant specification only discloses inducing multipotent neural stem cells for differentiation to oligodendrocytes by culturing said cells in the presence of GM-CSF. It fails to disclose whether IL-3, IL-5 alone or in combination of GM-CSF can produce oligodendrocyte from the multipotent neural stem cell culture. The Weiss declaration does not teach inducing neural differentiation for oligodendrocyte lineage other than infusing GM-CSF. Therefore, the teaching of the specification is limited in view of the broader breadth of instant claims.

The state of prior art and the level of predictability in the art

The prior art is silent on whether contacting a cell culture of neural stem cells with GM-CSF, IL-3, IL-5 or a combination of any of the factors would induce differentiation toward oligodendrocyte. In other words, the prior art does not teach GM-CSF, IL-3 or IL5 alone or in combination being oliogodendrocyte promoting factor. The prior art recognizes cells in the central nervous system produces and respond to a variety of cytokines including GM-CSF, IL-3 and IL-5, and the expression of corresponding specific receptor in such cells (see page 131, 1st col., Swada et al., Neuroscience Letters, 1993, Vol 160, pages 131-134, IDS). However, Sawada et al. discloses that oligodendrocytes express only receptor for IL-3, 4, 7, GM-CSF and M-CSF, no expression of IL-5 is observed in oligodendrocyte population (see Figure 2 on page 132). Mehler et al. (Int.J. Devl. Neuroscience. 1995, Vol. 13, No. 314, pages 213-240) further disclose that CNS stem cell favors neuronal lineage commitment and differentiation in the presence of IL-5, whereas bFGF, PDGF-AA, NT3, IGF1 and GP-130 receptor associated factor subclass favors oligodendrocyte lineage commitment and differentiation (See Table 1 on page 214). Evans et al. (Blood, 2002. Vol 100, no. 9, pages 3164-3174) demonstrates critical differences in IL-3R and GM-CSF R in the governing of cell fate although both receptor share the same β subunit, indicating α cytosolic domains can be ascribed specific function, not simply an ability to activate β subunit (see page 3173, 2nd col., last paragraph). Based on the teaching from the prior art, whether treating neural tissue with GM-CSF, IL-3 or IL-5 alone or in combination would result in producing oligodendrocytes is unpredictable.

Although the instant specification discloses that GM-CSF is able to enhance neural stem cell differentiation into oligodendrocyte lineage, it does not extend to the predictability whether IL-3 or IL-5 alone or in combination has the same function based on the knowledge in prior art.

The prior art teaches that IL-5 induces lineage commitment to neuronal cells, and that mature oligodendrocyte do not express IL-5 receptor. As such, whether combining IL-5 and GM-CSF would commit the neural stem cell to oligodendrocyte is unpredictable. Since IL-3 and GM-CSF each elicit different action in hematopoietic cells through their specific receptor, it is more likely than not that they would have different action in determine cell fate in neural tissue as well. Based on the limited teaching from the specification and the art recognized unpredictability in their action for neural stem cell lineage commitment, the claimed method is only enabled to the scope as indicated above. One of skilled in the art would have to engage in undue experimentation to practice the claimed method to the full scope.

Claims 1, 6-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement is set forth by 35 U.S.C. 112, first paragraph which states that the: "*specification* shall contain a written description of the invention. ..[emphasis added]." The written description requirement has been well established and characterized in the case law. A specification must convey to one of skill in the art that "as of the filing date sought, [the inventor] was in possession of the invention." See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in "possession" of the invention claimed by describing the invention with all of its claimed limitations "by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the

claimed invention." See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

In analyzing whether the written description requirement is met, it is first determined whether a representative number of species have been described by their complete structure. Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics. Claim 1 recites contacting the multipotent neural stem cell with "granulocyte-macrophage colony stimulating factor." The specification defines "granulocyte-macrophage colony stimulating factor" as any protein that shares at least 30% identity with the native human GM-CSF, and possesses a biological activity of the native human GM-CSF, which it binds to any known GM-CSF receptor (see page 11, lines 17-19, and page 12, lines 10-11). The claimed genus of GM-CSF encompasses a large number of polypeptides that may or may not have the biological function of stimulating neural stem cell proliferation and differentiation into oligodendrocytes. Although GM-CSF from a number of different species have already been identified in the prior art, relative to the claimed genus of polypeptides, it is only a small subset of the claimed polypeptides which is not a representative number of species that satisfied the entire genus. The specification only demonstrates the murine GM-CSF induces oliogodendrocyte differentiation in mouse neural stem cell. The specification does not any other polypeptide comprises 30% sequence identity to human GM-CSF (any polypeptide that comprises 44 amino acid identical to human GM-CSF sequence) which can bind to any GM-CSF receptor that possesses the same function. The specification fails to describe critical fragment of the human GM-CSF which is required for the function of induce oligodendrocyte lineage commitment. As such, the specification fails to provide sufficient

description to the claimed invention to reasonably convey one of skilled in the art that the inventor had possession of the invention at the time the invention was made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CELINE X. QIAN whose telephone number is (571)272-0777. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joe Woitach Ph.D. can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Celine X Qian Ph.D./
Primary Examiner, Art Unit 1636